BIOSCIENCES 741 - GENOMICS
FALL SEMESTER, 2015
BULL RUN HALL, ROOM 249
TUESDAY, 4:30 PM - 7:10 PM

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Summary: Biology reached a turning point in February, 2001, with the publication of the euchromatic portion of the human genome. Progress since then in genetics, medicine, biotechnology, pharmacology, and many other fields has been increasingly dependent on the data, techniques and concepts of genomics. The basic facts of biology rely upon the molecular anatomy of our chromosomes, just as basic facts of physiology rely upon the anatomy of our nerves and muscles. However, the volume and complexity of genomic sequence data pose significant problems of interpretation, which will occupy biologists for generations to come.

Prerequisites: Graduate standing, plus at least one undergraduate course in genetics and one undergraduate course in molecular biology.

Readings: There is one required textbook for this class: Pevsner (2009) *Bioinformatics and Functional Genomics* (2nd edition, Wiley). The assigned readings from this text are listed below. An additional text that may be helpful is Gibson and Muse (2009) *A Primer of Genome Science* (3rd edition, Sinauer, Sunderland, MA), which is available for purchase in the bookstore, and also will be on 2 hr reserve in the Mercer library throughout the semester. Additional readings from the primary research literature will be assigned, and are listed below. Most of these papers are available through the GMU library web site (library.gmu.edu). If not, copies will be posted on Blackboard.

Grading: Grades will be based on midterm (30%) and final (30%) examinations, plus attendance and active participation in class discussions (15%), an abstract of your term paper (5%) and the final draft of your term paper (20%). Midterm and final exams will be short essay, in-class, closed book exams. The midterm exam will cover the first half of the course; the final exam will cover the second half of the course. Midterm and final exams typically consist of about 5 questions, each of which requires an answer about one page in length. These exam questions will focus on the main points in the lectures and assigned readings, as identified by questions at the end of each chapter in the text, and plus Discussion Questions in the lecture notes (which will be posted on Blackboard). Students are expected to do the assigned readings before coming to class, and be prepared to participate in class discussions on these subjects. Makeup exams are not given in this course; excused absences from exams require prior permission from the instructor (that means a two-way conversation, not a voice mail or an e-mail). The use of cell phones (spoken or texting) during exams is not allowed.

As topics for term papers, each student will select a paper from the reading list, to be used as an initial focus for their term paper, and then choose a related focus (such as a hypothesis, controversy, or specific subfield) as the scope of their term paper. The abstract (150-300 words) will summarize and justify this specific focus. The final draft of the written term paper will be an expanded, critical discussion of the current scientific state of the art in the area of genomics. Term papers will be typed, double-spaced, including at least 15+ pages of text (plus an additional required title page, plus an additional required abstract page, plus additional required reference pages). Other items may be included (such as illustrations, quotes, acknowledgements, etc) but do not count towards the minimum length of the text. Your paper should cite at least 30 scientific papers (preferably more), all of which are included in your bibliography, and properly cited in your text. Please note that newspapers, internet web sites, course text books, etc. do not count as "scientific papers", and listing a paper in your bibliography without citing it does not count as a "citation". Plagiarism (copying text without proper attribution) is an Honor Code violation and will be prosecuted. However, you may paraphrase text from the scientific literature, provided that you immediately cite your source at the end of that sentence. The final version of your abstract should state your own critical conclusions [for example, advantages and disadvantages of particular approaches; which results and interpretations are (or are not) well supported; promising directions for the future, etc]. These conclusions should be justified (logically and with supporting evidence) in the text. Term papers and abstracts are due in class on the dates stated (see below), in paper printouts (not e-mail), with a 10% per day penalty for late papers.

Week 1 (September 1) Introduction to genomics

Pevsner text: pp. 525-543.

van Nimwegen, E. (2003) Scaling laws in the functional content of genomes. *Trends Genet*. **19**, 479-484.

Week 2 (September 8) Sequencing methods, BAC fingerprinting, physical maps and FISH

Pevsner text: pp. 544-554; 802-805.

Lander, E.S. *et al*. (2001) Initial sequencing and analysis of the human genome. *Nature* **409**, 860-921 (we will focus this week on pp. 860-875)

Week 3 (September 15) cDNA libraries, EST clusters, gene prediction and functional annotation

Pevsner text: pp. 161-174; 282-309; 555-559; 662-669.

Nekrutenko, A. (2004) Reconciling the numbers: ESTs versus protein-coding genes. *Mol. Biol. Evol*. **21**, 1278-1282.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* **409**, 860-921. (we will focus this week on pp. 894-903).

Week 4 (September 22) Bacterial genomes

Pevsner text: chapter 15.

Roach, D. J. et al. (2015) A year of infection in the intensive care unit: prospective whole genome sequencing of bacterial clinical isolates reveals cryptic transmissions and novel microbiota. PLOS Genet. 11(7), e1005413.

Chen, J. et al. (2015) Pathogenicity island-directed transfer of unlinked chromosomal virulence genes. Mol. Cell 57, 138-149.

Week 5 (September 29) Gene expression analysis

Pevsner text: pp. 309-323; 331-370.

Lenhard, B., et al. (2012) Metazoan promoters: emerging characteristics and insights into transcriptional regulation. Nat Rev Genet 13, 233-245.

Furey, T. S. (2012) ChIP-seq and beyond: new and improved methodologies to detect and characterize protein-DNA interactions. Nat Rev Genet 13, 840-852.

Week 6 (October 6) Alternative splicing

Wang, Z. and Burge, C. B. (2008) Splicing regulation: from a parts list of regulatory elements to an integrated splicing code. RNA 14, 802-813.

Kalsotra, A. and Cooper, T. A. (2011) Functional consequences of developmentally regulated alternative splicing. Nat Rev Genet 12, 715-729.

Davuluri, R. V. et al. (2008) The functional consequences of alternative promoter use in mammalian genomes. Trends Genet 24, 167-177.

Week 7 (October 13) Columbus Day – this week Monday classes meet on Tuesday, and Tuesday classes do not meet!

Week 8 (October 20) work on term paper (Society for Neuroscience meeting in Chicago)

Week 9 (October 27) Midterm Examination - covers weeks 1-6 (ABSTRACTS of term papers due today)

Week 10 (November 3) Proteomics

Pevsner text: chapters 10-11.

Schwanhäusser, B. et al. (2011) Global quantification of mammalian gene expression control. Nature 473, 337-342.

Maarten Altelaar, A. F. et al. (2013) Next-generation proteomics: towards an integrative view of proteome dynamics. Nat Rev Genet 14, 35-48.

Week 11 (November 10) The eukaryotic chromosome: noncoding and repetitive sequences, chromosome rearrangements and gene families

Pevsner text: pp. 47-75; chapter 16; pp. 773-778; pp. 808-811.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 879-885; 887-889).

Waterston, R.H., K. Lindblad-Toh, E. Birney et al. (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* **420**, 520-562.

Week 12 (November 17) Genetic polymorphisms, population genetics and human genetics

Pevsner text: pp. 778-782; pp. 825-832.

Bentley, D. B. (2003) DNA sequence variation of *Homo sapiens*. *Cold Spring Harbor Symp. Quant. Biol.* **68**, 55-63. (A PDF copy of this article will be posted on the course web site.)

Weischenfeldt, J. et al. (2013) Phenotypic impact of genomic structural variation: insights from and for human disease. Nat Rev Genet 14, 125-138.

Week 13 (November 24) The human genome: codon bias, gene density, GC content, recombination, CpG islands

Pevsner text: pp. 806-808; pp. 812-825.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 875-879; 885-887; 892-894).

Hinch, A. G. et al. (2011) The landscape of recombination in African Americans. Nature 476, 170-175.

Week 14 (December 1) Epigenetics – DNA methylation

Jones, P. A. (2012) Functions of DNA methylation: islands, start sites, gene bodies and beyond. Nat Rev Genet 13, 484-492.

Smith, Z. D. and Meissner, A. (2013) DNA methylation: roles in mammalian development. Nat Rev Genet 14, 204-220.

Branco, M. R. et al. (2012) Uncovering the role of 5-hydroxymethyl cytosine in the epigenome. Nat Rev Genet 13, 7-13.

Week 15 (December 8) Epigenetics - histone modifications.

Term papers due today! Late penalty is 10% per day!

Jin, C. et al. (2009) H3.3/H2A.Z double variant-containing nucleosomes mark 'nucleosome-free regions' of active promoters and other regulatory regions. Nat Genet 41, 941-945.

Ernst, J. et al. (2011) Mapping and analysis of chromatin state dynamics in nine human cell types. Nature 473, 43-49.

Greer, E. L. and Shi, Y. (2012) Histone methylation: a dynamic mark in health, disease and inheritance. Nat Rev Genet 13, 343-357.

December 15 - Final Exam - 4:30 pm to 7:15 pm. Covers weeks 10-15.